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RESEARCH ARTICLE

INCIDENTAL THYROID MALIGNANCY IN PATIENTS OPERATED FOR MULTINODULAR GOITER IN A TERTIARY CARE CENTRE IN KERALA

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Abstract

Background: Multinodulargoiter (MNG) is one of the most common thyroid disorders encountered in surgical practice and is traditionally regarded as a benign condition. However, increasing evidence suggests that a proportion of patients with apparently benign multinodulargoiter may harbor occult thyroid malignancy that remains undetected during preoperative evaluation. Limitations of diagnostic modalities such as ultrasonography and fine needle aspiration cytology (FNAC), particularly in the setting of multiple nodules, contribute to this diagnostic challenge.Identification of incidental thyroid malignancy has significant implications for surgical planning, postoperative management, and long-term follow-up.

Aim: To identify the incidence of incidental thyroid malignancy in patients undergoing total thyroidectomy for multinodulargoiter.

Objectives: To estimate the proportion of thyroid malignancies detected incidentally on histopathological examination following thyroidectomy for multinodulargoiter and to assess the demographic and clinical characteristics of these patients.

Materials and Methods: A prospective observational study was conducted in the Department of General Surgery at Government Medical College, Kozhikode, over a period of twelve months. A total of 106 patients aged above 13 years who underwent total thyroidectomy for multinodular goiter were included.Patients with a preoperative diagnosis of thyroid malignancy or features suggestive of invasive disease were excluded.Clinical details,biochemical parameters, ultrasonographic findings ,FNAC reports, and postoperative histopathological results were recorded and analyzed using appropriate statistical methods.

Introduction:-

Multinodulargoiter (MNG) is a common endocrine disorder characterized by the presence of multiple nodules within the thyroid gland and represents one of the most frequent indications for thyroid surgery worldwide. The

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condition is particularly prevalent in iodine-deficient regions, but it is also commonly encountered in iodine-sufficient areas due to a combination of genetic, environmental, and hormonal factors. Traditionally, multinodulargoiter has been regarded as a benign disease process, with malignancy thought to occur less frequently than in solitary thyroid nodules. However, emerging evidence has challenged this long-held belief.Thyroid cancer is the most common malignancy of the endocrine system, with a steadily rising global incidence over the past few decades. Differentiated thyroid carcinomas, particularly papillary thyroid carcinoma, account for the majority of cases and generally have an excellent prognosis when detected early. The increasing detection of thyroid malignancies has been attributed partly to improved diagnostic techniques and increased use of imaging modalities, leading to the identification of subclinical and incidental cancers. Despite these advances, the detection of malignancy in the setting of multinodulargoiter remains problematic.

Fine needle aspiration cytology (FNAC) is widely accepted as the primary diagnostic tool for evaluating thyroid nodules. While FNAC has high sensitivity and specificity for solitary nodules, its diagnostic accuracy diminishes in multinodulargoiter due to sampling errors, difficulty in selecting the most suspicious nodule, and the presence of heterogeneous pathology within the gland. Similarly, ultrasonography, although invaluable in risk stratification through features such as hypoechogenicity, microcalcifications, and irregular margins, may fail to reliably differentiate benign from malignant nodules when multiple nodules coexist.As a result, a subset of patients undergoing thyroidectomy for apparently benign multinodulargoiter are found to have incidental thyroid malignancy on final histopathological examination. These incidental carcinomas are often small, well-differentiated, and clinically silent, yet their detection has important implications for postoperative management, including the need for completion thyroidectomy, radioactive iodine therapy, and long-term surveillance.

The reported incidence of incidental thyroid malignancy in multinodulargoiter varies widely in the literature, ranging from as low as 5% to over 30% in different populations. This variability may be attributed to differences in geographic location, iodine intake, genetic factors, surgical indications, extent of thyroidectomy, and histopathological scrutiny. Indian studies have also demonstrated considerable heterogeneity in reported malignancy rates, highlighting the need for region-specific data.In a tertiary care setting, where patients often present late with long-standing disease and large goiters, the risk of occult malignancy assumes greater clinical significance. Understanding the true incidence of incidental thyroid malignancy in multinodulargoiter is essential for optimizing surgical strategies, counseling patients regarding risks and prognosis, and developing more effective preoperative diagnostic protocols.This prospective observational study was therefore undertaken at a tertiary care centre in Kerala to evaluate the incidence of incidental thyroid malignancy in patients undergoing total thyroidectomy for multinodulargoiter and to analyze their demographic and clinical characteristics.

Review of Literature:-

Multinodular Goiter: Epidemiology and Clinical Significance:-

Multinodular goiter (MNG) represents a late stage in the natural history of thyroid enlargement and is characterized by structural and functional heterogeneity of thyroid follicular cells. The condition is common worldwide and constitutes a major burden on endocrine and surgical services, particularly in developing countries. Epidemiological studies suggest that the prevalence of palpable thyroid nodules ranges from 4–7% in the general population, while ultrasonographic screening detects nodules in up to 60–70% of adults. Multinodulargoiter is more frequently observed in females and its prevalence increases with age.Iodine deficiency has traditionally been considered the most important etiological factor in the development of multinodulargoiter. However, the persistence of MNG in iodine-sufficient areas indicates that additional factors such as genetic predisposition, environmental goitrogens, smoking, hormonal influences, and altered thyroid growth factor signaling also play a significant role. Long-standing stimulation by thyroid-stimulating hormone (TSH) leads to follicular hyperplasia, followed by nodular transformation due to clonal expansion of genetically altered thyrocytes.Clinically, multinodulargoiter is often asymptomatic and may remain undetected for years. Patients typically present with a slowly enlarging neck mass, cosmetic concerns, or compressive symptoms such as dysphagia, dyspnea, and voice changes in advanced cases. Although traditionally considered benign, increasing attention has been directed toward the malignant potential of multinodulargoiter.

Thyroid Malignancy: Global and Indian Perspective:-

Thyroid carcinoma is the most common endocrine malignancy and accounts for approximately 3–4% of all newly diagnosed cancers worldwide. The incidence of thyroid cancer has increased steadily over the past few decades, largely due to improved detection of small, subclinical tumors. Papillary thyroid carcinoma (PTC) is the most

common histological subtype, accounting for nearly 80–85% of all thyroid malignancies, followed by follicular thyroid carcinoma (FTC), medullary carcinoma, and anaplastic carcinoma.In India, thyroid cancer exhibits a clear female predominance, with reported incidence rates of approximately 3.9% in women and 0.9% in men. Regional variations exist, influenced by iodine status, dietary habits, and healthcare access. Despite the rising incidence, thyroid cancer generally carries an excellent prognosis, particularly differentiated thyroid carcinomas, with 10-year survival rates exceeding 90%.The challenge in thyroid oncology lies not in treatment but in accurate and timely diagnosis, especially in patients with multinodulargoiter, where malignancy may remain clinically occult.

Solitary Thyroid Nodule Versus MultinodularGoiter:-

Historically, solitary thyroid nodules (STN) have been regarded as carrying a higher risk of malignancy compared to multinodulargoiter. This belief has influenced clinical decision-making for decades. Several early studies reported malignancy rates of 10–20% in solitary nodules, whereas multinodulargoiter was considered relatively low risk.

However, more recent evidence suggests that the presence of multiple nodules does not confer protection against malignancy. In fact, malignancy can arise in any nodule within a multinodular gland, including nodules that appear clinically and radiologically benign. Some studies have demonstrated comparable malignancy rates between STN and MNG, while others report only a modestly lower risk in MNG.A large systematic review and meta-analysis by Rahman et al., which included over 50,000 patients, demonstrated that multinodulargoiter was associated with a lower risk of thyroid cancer compared to solitary nodules, with an odds ratio of 0.76. However, the authors emphasized that malignancy was still present in a significant proportion of MNG patients, underscoring the need for vigilance.

Incidental Thyroid Malignancy:-

Incidental thyroid malignancy refers to thyroid cancer that is discovered unexpectedly on histopathological examination following surgery performed for benign thyroid disease. With the increasing use of total thyroidectomy for multinodulargoiter, the detection of incidental malignancies has risen.Incidental carcinomas are typically small, well-differentiated tumors, most commonly papillary thyroid microcarcinomas measuring less than 1 cm in diameter. These tumors are often clinically silent, lack aggressive features, and are not suspected preoperatively. Despite their indolent nature, their identification has important implications for postoperative management, including decisions regarding radioactive iodine therapy and long-term surveillance.Reported incidence rates of incidental thyroid malignancy in multinodulargoiter vary widely, ranging from 5% to as high as 35% in different series. This wide variation reflects differences in study design, population characteristics, extent of surgery, and histopathological examination protocols.

Role and Limitations of Ultrasonography:-

High-resolution ultrasonography is the imaging modality of choice for evaluating thyroid nodules. It provides valuable information regarding nodule size, echogenicity, margins, vascularity, and presence of microcalcifications. The development of standardized reporting systems such as the Thyroid Imaging Reporting and Data System (TI-RADS) has improved risk stratification and guided the selection of nodules for FNAC.However, in the setting of multinodulargoiter, ultrasonography has inherent limitations. The presence of multiple nodules makes it difficult to identify the most suspicious lesion, and malignant nodules may lack classical sonographic features. Additionally, diffuse architectural distortion and coexisting thyroiditis may obscure subtle malignant characteristics.Studies have shown that a significant proportion of malignant nodules in multinodulargoiter do not exhibit high-risk ultrasonographic features, leading to false reassurance and underdiagnosis.

Fine Needle Aspiration Cytology in MultinodularGoiter:-

Fine needle aspiration cytology is widely regarded as the gold standard initial diagnostic test for thyroid nodules. When applied to solitary nodules, FNAC demonstrates high sensitivity and specificity. However, its performance in multinodulargoiter is less reliable.Sampling error is a major limitation of FNAC in MNG, as only selected nodules are aspirated, potentially missing malignant foci in unsampled areas. Furthermore, cytological interpretation can be challenging in nodular hyperplasia and follicular-patterned lesions, where architectural features necessary for diagnosing malignancy cannot be assessed.Several studies have reported that FNAC fails to detect a substantial proportion of malignancies subsequently identified on histopathology in MNG patients. This diagnostic gap contributes significantly to the phenomenon of incidental thyroid malignancy.

Histopathological Patterns of Incidental Malignancy:-
Papillary thyroid carcinoma is consistently reported as the most common histological type of incidental malignancy detected in multinodulargoiter. Follicular carcinoma and Hürthle cell carcinoma are less frequent. Papillary microcarcinomas constitute a large proportion of these incidental findings.Although papillary microcarcinomas generally have an excellent prognosis, certain features such as multifocality, extrathyroidal extension, and lymphovascular invasion may increase the risk of recurrence. Consequently, accurate histopathological evaluation of thyroidectomy specimens is essential to guide postoperative management.

Indian Studies on Incidental Thyroid Malignancy:-
Indian literature on incidental thyroid malignancy in multinodulargoiter is limited but growing. Several hospital-based studies have reported malignancy rates ranging from 6% to 15% in patients operated for clinically benign goiter. Differences in iodine status, patient demographics, and healthcare-seeking behavior may account for these variations.Studies from tertiary care centers highlight that a significant proportion of patients present late with long-standing goiters, yet malignancy remains clinically unsuspected preoperatively. These findings emphasize the importance of region-specific data to guide surgical decision-making in the Indian context.

Rationale for the Present Study:-
Given the variability in reported malignancy rates and the diagnostic limitations of FNAC and ultrasonography in multinodulargoiter, there is a need for institution-specific data to better understand the true incidence of incidental thyroid malignancy. Such data are essential for informing surgical strategies, optimizing patient counseling, and identifying areas for improvement in preoperative risk assessment.The present study was undertaken in a tertiary care centre in Kerala to evaluate the incidence of incidental thyroid malignancy in patients undergoing total thyroidectomy for multinodulargoiter and to contribute to the existing body of literature from the Indian subcontinent

Materials and Methods:-

Study Design:-
This study was conducted as a prospective observational study aimed at determining the incidence of incidental thyroid malignancy in patients undergoing surgery for multinodulargoiter. A prospective design was chosen to ensure systematic data collection and uniform evaluation of patients during the study period.

Study Setting:-
The study was carried out in the Department of General Surgery, Government Medical College, Kozhikode, a tertiary care referral centre catering to patients from both urban and rural regions of North Kerala. The institution routinely manages a large volume of thyroid disorders, making it an appropriate setting for studying multinodulargoiter and its associated complications.

Study Period:-
The study was conducted over a period of twelve months, following approval from the Institutional Ethics Committee.

Study Population:-
The study population comprised patients diagnosed with multinodulargoiter who underwent total thyroidectomy during the study period.

Sample Size:-
The sample size was calculated using the formula:
$n= 4pq/d^2$
Where:
p = prevalence of malignancy in multinodulargoiter from a reference study (31%)
q = 100 − p = 69
d = absolute precision (9)
$n=4x31x69/9^2=105.6$
Accordingly, a minimum sample size of 106 patients was included in the study.

Inclusion Criteria:-
All patients aged above 13 years undergoing total thyroidectomy for multinodulargoiter were included. Indications for surgery included:
Toxic multinodulargoiter with failure of medical management Multinodulargoiter with compressive symptoms such as dysphagia or dyspnea Nodules classified as TI-RADS 1 to TI-RADS 3 Surgery performed for cosmetic reasons

Exclusion Criteria:-
Patients were excluded from the study if they had:
A preoperative diagnosis of thyroid malignancy TI-RADS 4 or higher nodules Clinical features suggestive of invasive disease such as hoarseness of voice or fixation to surrounding structures

Data Collection:-
A structured proforma was used to collect demographic data, clinical history, duration of disease, comorbidities, and family history of thyroid disorders. Preoperative evaluation included thyroid function tests, ultrasonography findings, and fine needle aspiration cytology (FNAC) reports. All patients underwent total thyroidectomy, and the resected specimens were subjected to detailed histopathological examination.

Statistical Analysis:-
Data were entered into Microsoft Excel and analyzed using Statistical Package for the Social Sciences (SPSS) software. Quantitative variables were expressed as mean and standard deviation, while qualitative variables were expressed as frequencies and percentages. Associations between categorical variables were assessed using the Chi-square test. A p value of less than 0.05 was considered statistically significant.

Ethical Considerations:-
Institutional Ethics Committee approval was obtained prior to commencement of the study. Written informed consent was taken from all participants, and confidentiality of patient information was strictly maintained.

Results:-

Demographic Profile:-
A total of 106 patients were included in the study. The mean age of the study population was 49.37 ± 12.15 years, with patient ages ranging from 23 to 77 years. The majority of patients belonged to the middle-aged group, reflecting the chronic and slowly progressive nature of multinodulargoiter.

Gender Distribution:-
There was a marked female predominance in the study population. Of the 106 patients, 95 (89.62%) were females and 11 (10.38%) were males, consistent with the known higher prevalence of thyroid disorders among women.

Comorbidities:-
Nearly half of the patients (45.28%) had no associated comorbid conditions. Among those with comorbidities, hypertension was the most common (14.15%), followed by coronary artery disease (10.38%) and diabetes mellitus (9.43%). The presence of comorbidities did not show a significant association with the occurrence of malignancy.

Duration of Disease:-
The mean duration of multinodulargoiter was 102.18 ± 26.79 months, indicating a long-standing disease course in most patients. This finding highlights the indolent progression of multinodulargoiter and the tendency of patients to seek medical attention late.

Family History:-
A positive family history of thyroid disease was reported in only one patient (0.94%), suggesting that familial predisposition was uncommon in the present study population.

Thyroid Function Status:-
Preoperative thyroid function tests revealed that 78.30% of patients were euthyroid. Hyperthyroidism was observed in 15.09%, while 6.60% were hypothyroid. Thyroid function status did not show a significant correlation with the presence of malignancy.

Prior Treatment for Thyroid Disease:-
A history of prior medical treatment for thyroid disease was noted in 21.70% of patients, while the remaining 78.30% had not received any prior treatment.

Nodule Characteristics:-
The mean size of the largest palpable nodule was 33.72 ± 12.41 mm, with sizes ranging from 3.3 mm to 65.1 mm. On clinical examination, the majority of nodules were firm in consistency (98.11%), while only 1.89% were hard. Hard nodules were not consistently associated with malignancy.

Cervical Lymph Nodes and Retrosternal Extension:-
Palpable cervical lymph nodes were noted in only one patient (0.94%), and retrosternal extension was observed in 3.77% of patients. These features were uncommon, reflecting the benign clinical presentation in most cases.

Ultrasonographic Findings:-
Ultrasonography revealed bilateral lobe involvement in 87.74% of patients, while unilateral involvement was seen in 12.26%. Features suggestive of local infiltration were present in only 5.66% of cases.

FNAC Findings:-
FNAC revealed features of thyroiditis in 2.83% of patients, while the majority showed benign cytological patterns. FNAC failed to identify malignancy in patients who were later found to have carcinoma on histopathological examination.

Incidence of Incidental Thyroid Malignancy:-
Histopathological examination of the thyroidectomy specimens revealed incidental thyroid malignancy in 7 patients, yielding an incidence of 6.60%. All malignant cases were diagnosed as papillary thyroid carcinoma. The remaining 93.40% of patients had benign multinodulargoiter.

Discussion:-
Multinodulargoiter has long been regarded as a benign thyroid disorder, particularly in iodine-sufficient regions. However, increasing evidence suggests that a subset of patients with multinodulargoiter may harbor occult thyroid malignancy that remains undetected during preoperative evaluation. The present study was undertaken to determine the incidence of incidental thyroid malignancy in patients undergoing total thyroidectomy for multinodulargoiter and to analyze associated demographic and clinical factors in a tertiary care setting.In the present study, incidental thyroid malignancy was detected in 6.6% of patients. All malignant cases were identified as papillary thyroid carcinoma on final histopathological examination. This finding reinforces the concept that multinodulargoiter cannot be universally considered a benign condition and that malignancy may coexist despite apparently benign clinical, radiological, and cytological features.

Comparison with Other Studies:-
The incidence of incidental thyroid malignancy reported in the literature varies widely. Luo et al. reported a malignancy rate of approximately 31% in patients with multinodulargoiter undergoing thyroidectomy, with nearly half of these tumors being microcarcinomas. Similarly, Ajarma et al. observed a malignancy rate of 29.2% in multinodulargoiter patients, which was lower than that observed in solitary thyroid nodules but still clinically significant.In contrast, the incidence observed in the present study is considerably lower. This discrepancy may be attributed to several factors, including regional differences in iodine intake, genetic susceptibility, patient selection criteria, and the exclusion of higher-risk nodules (TI-RADS 4 and above). Additionally, differences in surgical indications and the extent of histopathological scrutiny may influence reported malignancy rates.Indian studies have reported malignancy rates ranging from 6% to 15% in patients operated for clinically benign goiters. The findings of the present study align closely with the lower end of this spectrum, suggesting that the risk profile in this population may be relatively conservative compared to some international cohorts.

Demographic and Clinical CorrelatesThe study population demonstrated a strong female predominance, consistent with the known epidemiology of thyroid disorders. The mean age of patients was approximately 49 years, reflecting the chronic and slowly progressive nature of multinodulargoiter. No statistically significant association was found between age, gender, duration of disease, or presence of comorbidities and the occurrence of malignancy.The majority of patients were euthyroid at presentation, and thyroid function status did not correlate with malignancy

risk. This finding supports existing evidence that thyroid hormone levels alone are not reliable predictors of malignancy in multinodulargoiter.

Role of Ultrasonography and FNAC:-
Ultrasonography remains a cornerstone in the evaluation of thyroid nodules, particularly with the advent of standardized reporting systems such as TI-RADS. However, in the setting of multinodulargoiter, the diagnostic utility of ultrasonography is limited by the presence of multiple nodules with heterogeneous features. In the present study, ultrasonographic findings did not reliably predict malignancy.Fine needle aspiration cytology is widely regarded as the gold standard for preoperative evaluation of thyroid nodules. Nevertheless, its limitations are particularly evident in multinodulargoiter, where sampling error and difficulty in selecting the most suspicious nodule reduce diagnostic accuracy. In this study, FNAC failed to identify malignancy in all patients subsequently diagnosed with papillary carcinoma on histopathology, underscoring the inherent limitations of FNAC in this context.

Histopathological Findings and Clinical Implications:-
All malignant cases identified in this study were papillary thyroid carcinoma, the most common and least aggressive form of differentiated thyroid cancer. Although papillary carcinomas generally have an excellent prognosis, their incidental detection has important clinical implications. The identification of malignancy may necessitate additional interventions such as radioactive iodine therapy, long-term surveillance, and patient counseling regarding recurrence risk.The findings of this study highlight the importance of meticulous histopathological examination of thyroidectomy specimens, even when surgery is performed for ostensibly benign disease.

Limitations:-

Single-Center Study:
As this study was conducted at a single tertiary care center, the findings may not be generalizable to all populations.

Limited Sample Size:
Although adequately powered for incidence estimation, the relatively small sample size limits subgroup analysis and detection of subtle associations.

Lack of Long-Term Follow-Up:
The study did not include long-term follow-up to assess recurrence rates or long-term outcomes of patients with incidental malignancy.

Diagnostic Constraints:
Advanced diagnostic modalities such as molecular testing and standardized TI-RADS scoring were not incorporated, which may have improved preoperative risk stratification.

Conclusion:-

The present study demonstrates that a clinically significant proportion of patients undergoing total thyroidectomy for multinodulargoiterharbor incidental thyroid malignancy, with an incidence of 6.6% in the study population. Despite benign preoperative evaluation, malignancy—most commonly papillary thyroid carcinoma—may remain undetected until histopathological examination.These findings underscore the limitations of ultrasonography and FNAC in excluding malignancy in multinodulargoiter and highlight the need for careful surgical decision-making and comprehensive postoperative histopathological analysis. Multinodulargoiter should not be regarded as an entirely benign entity, and clinicians must maintain a high index of suspicion, particularly in long-standing disease.Future studies involving larger, multicenter cohorts and incorporation of advanced diagnostic tools are warranted to refine risk stratification and optimize management strategies for patients with multinodulargoiter.

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